Welcome to the 76th issue of *HIV This Week*! In this issue, we cover the following topics:

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   - Technical innovations can overcome silos in HIV monitoring & evaluation: can they strengthen health systems?

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   - Similar HIV-free infant survival whether breastfeeding or formula feeding when Rwandan mothers are on antiretroviral treatment

3. **Treatment**
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   - Is UNGASS reporting increasing civil society participation in national HIV responses?

5. **Epidemiology**
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1. Health systems strengthening

“Talkin' about a revolution”: How electronic health records can facilitate the scale-up of HIV care and treatment and catalyze primary care in resource-constrained settings.


Health care for patients with HIV infection in developing countries has increased substantially in response to major international funding. Scaling up treatment programs requires **timely data on the type, quantity, and quality of care being provided**. Increasingly, such programs are turning to **electronic health records** to provide these data. The authors describe how a medical school in the United States and another in Kenya collaborated to develop and implement an electronic health records system in a large HIV care program in western Kenya. These data were used to manage patients, providers, and the program itself as it grew to encompass 18 sites serving more than 90,000 patients. Lessons learned have been applicable beyond HIV to include primary care, chronic disease management, and community-based health screening and disease prevention programs. **Electronic health records will be key to providing the highest possible quality of care for the funds developing countries can commit to health care.** Public, private, and academic partnerships can facilitate the development and implementation of electronic health records in resource-constrained settings.


Editors’ note: Quality health care depends, among other things, on collecting, analysing, and using timely health information. Well managed health information management systems can help programme managers plan deployment of personnel, avoid drug stockouts, and maximise resource use. But, first and foremost, meeting clinicians’ requirements for complete and accurate data is key to ensuring high-quality care for patients. Electronic medical records using unique identifiers while protecting patient confidentiality and data security help coordinate care across multiple venues and specialities. Patients can be notified quickly of drug recalls or eligibility for novel treatments and can use their laminated personal card to access care throughout the health system. Investment in electronic health records for patients in antiretroviral treatment programmes is reaping benefits in low- and middle-income countries that are expanding data capture and management to support the scale up of efficient, effective clinical services for other conditions. We really are “talkin’ about a revolution”!


Program monitoring and evaluation has the potential to be a cornerstone of health systems strengthening and of evidence-informed implementation and scale-up of HIV-related services in resource-limited settings. The authors discuss common challenges to monitoring and evaluation systems used in the rapid scale-up of HIV services as well as innovations that may have relevance to systems used to monitor, evaluate, and inform health systems strengthening. These include (1) **Web-based applications** with decentralized data entry and real-time access to summary reporting; (2) **timely feedback** of information to site and district staff; (3) **site-level integration** of traditionally siloed program area indicators; (4) **longitudinal tracking** of program and site characteristics; (5) **geographic information systems**; and (6) use of routinely collected aggregate data for **epidemiologic analysis and operations research**. Although conventionally used in the context of vertical programs, these approaches can form a foundation on which data relevant to other health services and systems can be layered, including **prevention services, primary care, maternal-child health, and chronic disease management**. Guiding principles for sustainable national monitoring and evaluation systems include **country-led development and**
ownership, support for national programs and policies, interoperability, and employment of an open-source approach to software development.

For full text access click here:  http://journals.lww.com/jaids/toc/2009/11011

Editors’ note: This article starts with a diagnosis of the challenge of providing timely and useful feedback to key staff at individual health facilities when information is hand tallied from paper-based sources and reported up to district, regional, national, and international agencies on schedules that reflect the latter’s needs. When the objective is continuous improvement of quality, scale, equity, and impact of services, the benefits of web-based real-time systems using solar powered mobile phones for data entry (such as Rwanda is developing) are evident. Overcoming silos in HIV monitoring and evaluation systems, each one designed for its own programme (e.g. antiretroviral treatment, prevention of mother-to-child transmission, voluntary counselling and testing), is key to moving forward to systems that integrate disease- or programme-specific data within broader primary care.

2. Infant feeding


The main aim of this study was to reduce breast-milk transmission of HIV-1 by treating HIV-1-infected women with antiretroviral therapy (ART) during breastfeeding. Mitra Plus was an open-label, nonrandomized, prospective cohort study. HIV-1-infected pregnant women in Dar es Salaam were treated with zidovudine (ZDV) + lamivudine (3TC) + nevirapine (NVP). NVP was later replaced by nevirapine for mothers with CD4 cell counts >200 cells per microlitre or with adverse reaction to NVP. Antiretroviral therapy was initiated at 34 weeks of gestation. For women with symptomatic HIV infection or CD4 cell counts below 200 cells per microlitre, antiretroviral therapy was started earlier if possible. Treatment of the mothers was stopped at 6 months except for those mothers who needed antiretroviral therapy for their own health. The infants received ZDV + 3TC for 1 week after birth. Mothers were advised to exclusively breastfeed and to wean abruptly between 5 and 6 months. Transmission of HIV-1 was analyzed using the Kaplan-Meier survival technique. Cox regression was used for comparison with the breastfeeding population of the Petra trial arm A. There were 441 infants included in the analysis of HIV-1 transmission. The cumulative transmission of HIV-1 was 4.1 % [95% confidence interval (CI): 2.2 to 6.0] at 6 weeks, 5.0% (95% CI: 2.9 to 7.1) at 6 months, and 6.0% (95% CI: 3.7 to 8.3) at 18 months after delivery. The cumulative risk of HIV transmission between 6 weeks and 6 months was 1.0% and between 6 months and 18 months 1.1%. The cumulative HIV infection or death rate was 8.6% (95% CI: 6.0 to 11.2) at 6 months and 13.6% (95% CI: 10.3 to 16.9) at 18 months after delivery. Viral load at enrolment and duration of antiretroviral therapy before delivery were significantly associated with transmission but CD4 cell count at enrolment was not. The median time of breastfeeding was 24 weeks. The transmission in the Mitra Plus study was about half of the transmission in the breastfeeding population in the Petra trial arm A at 6 months after delivery (adjusted relative hazard = 0.49, P < 0.001). The combined outcome HIV infection or death was significantly lower in the Mitra Plus study than in the breastfeeding population in the Petra trial arm A at 18 months (adjusted relative hazard = 0.61, P = 0.007). NVP-related mucocutaneous rash was demonstrated in 6.5% of 429 NVP-exposed women. The incidence of NVP-related grade 3 or 4 hepatotoxicity was low (0.5%). Antiretroviral therapy given to HIV-infected mothers in late pregnancy and during breastfeeding resulted in a low postnatal HIV transmission similar to that previously demonstrated in the Mitra study in Dar es Salaam using infant prophylaxis with 3TC during breastfeeding. The extended maternal prophylaxis with antiretroviral therapy for prevention of mother-to-child transmission of HIV-1 for breastfeeding mothers who do not need antiretroviral therapy for their own health should be further evaluated and compared with the use of infant postnatal antiretroviral prophylaxis regarding safety and cost-effectiveness.
Editors’ note: These Mitra Plus study findings from Tanzania of low HIV transmission through breastfeeding when mothers receive antiretroviral treatment, whether they need it for their own health or not, may well have informed the new WHO ‘rapid advice’ documents released last week. Although the option remains (Option A) to provide AZT only from as early as 14 weeks of pregnancy, followed by AZT and 3TC during labour and delivery and for 7 days postpartum - with breastfeeding babies then receiving nevirapine until one week after all exposure to breast milk has ended – a new option called Option B has emerged. It includes maternal triple antiretroviral prophylaxis from as early as 14 weeks and continuing until 1 week after all exposure of the infant to breast milk ends. Changes such as these will bring us closer to the goal of virtually eliminating mother-to-child transmission of HIV.

Breastfeeding with maternal antiretroviral therapy or formula feeding to prevent HIV postnatal mother-to-child transmission in Rwanda.


The aim of the study was to assess the 9-month HIV-free survival of children with two strategies to prevent HIV mother-to-child transmission in a nonrandomized interventional cohort study. Four public health centres in Rwanda enrolled participants between May 2005 and January 2007. All consenting HIV-infected pregnant women were included. Women could choose the mode of feeding for their infant: breastfeeding with maternal antiretroviral therapy for 6 months or formula feeding. All received antiretroviral therapy from 28 weeks of gestation.

Nine-month cumulative probabilities of HIV transmission and HIV-free survival were determined using the Kaplan-Meier method and compared using the log-rank test. Determinants were analysed using a Cox model analysis. Of the 532 first-liveborn infants, 227 (43%) were breastfeeding and 305 (57%) were formula feeding. Overall, seven (1.3%) children were HIV-infected of whom six were infected in utero. Only one child in the breastfeeding group became infected between months 3 and 7, corresponding to a 9-month cumulative risk of postnatal infection of 0.5% [95% confidence interval (CI) 0.1-3.4%; P = 0.24] with breastfeeding. Nine-month cumulative mortality was 3.3% (95% CI 1.6-6.9%) in the breastfeeding arm group and 5.7% (95% CI 3.6-9.2%) for the formula feeding group (P = 0.20). HIV-free survival by 9 months was 95% (95% CI 91-97%) in the breastfeeding group and 94% (95% CI 91-96%) for the formula feeding group (P = 0.66), with no significant difference in the adjusted analysis (adjusted hazard ratio for breastfeeding: 1.2 (95% CI 0.5-2.9%)). Maternal antiretroviral therapy while breastfeeding could be a promising alternative strategy in resource-limited countries.

Editors’ note: This study enrolled 562 HIV-positive pregnant women who were placed on antiretroviral treatment at 28 weeks of pregnancy regardless of CD4 count. Those who decided to formula feed stopped antiretroviral treatment after their baby’s birth if they were not eligible in Rwanda (less than 350 CD4 count) and those who decided to breastfeed continued antiretroviral treatment until 1 month after weaning their babies at 6 months of age and then stopped taking antiretroviral drugs if they were not eligible for treatment. All babies received a backbone of AZT and 3TC for seven days after they stopped being exposed to maternal antiretroviral drugs through the placenta or through breast milk to reduce the risk of resistance to the third drug (nevirapine or efavirenz). There was no difference in HIV-free survival and, amazingly, there was no significant difference in the mortality by infant feeding mode (3.3% versus 5.7%) although virtually all studies in low- and middle-income countries have shown higher mortality with formula feeding. This may be because mothers received education and good follow-up and care, regardless of the feeding option they chose. The bottom line is that the risk of HIV transmission during breastfeeding is minimal when mothers are on antiretroviral treatment, regardless of CD4 count.
3. Treatment

Antiretroviral therapy in antenatal care to increase treatment initiation in HIV-infected pregnant women: a stepped-wedge evaluation.


The objective of this study was to evaluate whether providing antiretroviral therapy (ART) integrated in antenatal care clinics resulted in a greater proportion of treatment-eligible women initiating antiretroviral therapy during pregnancy compared with the existing approach of referral to antiretroviral therapy. The evaluation used a stepped-wedge design and included all HIV-infected, antiretroviral therapy-eligible pregnant women in eight public sector clinics in Lusaka district, Zambia. The main outcome indicators were the proportion of treatment-eligible women enrolling into HIV care while pregnant and within 60 days of HIV diagnosis and proportion initiating antiretroviral therapy during pregnancy. Adjusted odds ratios (AORs) and confidence intervals (CIs) for enrolment and initiation proportions were estimated through a logistic regression model accounting for clinical site cluster and time effects. Between 16 July 2007 and 31 July 2008, 13 917 women started antenatal care more than 60 days before the intervention rollout and constituted the control cohort; 17 619 started antenatal care after antiretroviral therapy integrated into antenatal care and constituted the intervention cohort. Of the 1566 patients found eligible for antiretroviral therapy, a greater proportion enrolled while pregnant and within the 60 days of HIV diagnosis in the intervention cohort (376/846, 44.4%) compared with the control cohort (181/716, 25.3%), adjusted odds ratio 2.06, 95% CI (1.27-3.34); and initiated antiretroviral therapy while pregnant in the intervention cohort (278/846, 32.9%) compared with the control cohort (103/716, 14.4%), adjusted odds ratio 2.01, 95% CI (1.37-2.95). An integrated antiretroviral therapy in antenatal care strategy doubled the proportion of treatment-eligible women initiating antiretroviral therapy while pregnant.

For access to abstract click here: http://www.ncbi.nlm.nih.gov/pubmed/19809271

Editors’ note: This step-wedged evaluation design had all 8 participating clinics starting to collect data at the same time while providing the standard of care, i.e. referral to antiretroviral treatment services. Then one by one, each clinic crossed over to the intervention arm with antiretroviral services being provided in the antenatal care setting. This design allowed each clinic to act as its own control, providing patients to both arms, while also controlling for time trends by allowing comparisons across clinics at fixed points in time. Even though the treatment clinics were located on the same premises as the antenatal care clinics and local peer educators provided education and support to eligible women and offered to escort them to the treatment clinic, the percentage of treatment-eligible pregnant women initiating antiretroviral treatment more than doubled when antiretroviral treatment services were integrated into antenatal care. The lessons from this study can be applied to tuberculosis clinics and other services. Locating services together only goes so far in meeting patient needs and integration can make a big difference to uptake.

4. Civil society responses

Community Involvement in HIV and Tuberculosis Research.

Harrington M. J Acquir. Immune Defic Syndr. 2009; Nov:52(S2)

Since advent of the HIV pandemic in the 1980s, affected communities and individuals living with HIV have played key roles in leading the response to the crisis. Achievements of the HIV treatment activist movement include persuading the US Food and Drug Administration to allow expanded access to experimental treatments for those unable to enter controlled clinical trials; accelerated approval of anti-HIV drugs based on surrogate markers such as CD4 cell and HIV RNA changes; and the involvement of people with HIV and their advocates throughout the research system, including in the design, conduct, and evaluation of clinical trials. HIV treatment activists have adapted these skills to tackle tuberculosis (TB) research and programs. Considering the dearth of adequate diagnostic, treatment, and preventive interventions to control
TB among people with HIV, the experiences and efforts of HIV activists are vital to accelerate research and development of new diagnostics, drugs, and vaccines to identify, cure, and prevent TB, especially among people living with HIV. Advocacy to implement World Health Organization collaborative HIV/TB activities and to reduce TB’s toll among people with HIV provides a case study of how scale-up of HIV and TB programs contributes to health system strengthening.

For full text access click here:
http://journals.lww.com/jaids/Fulltext/2009/11011/Community_Involvement_in_HIV_and_Tuberculosis.18.aspx

Editors’ note: This ‘must read’ article presents a succinct history of the HIV treatment activist movement, underscoring the informed and relentless pressure that accelerated the pace of research and development for novel antiretroviral drugs. Community activists used mass media and the internet, political lawsuits and legislation, public demonstrations and civil disobedience, and coalition-building and other strategies to influence both the speed and conduct of treatment research. The article describes the gains made and the challenges ahead, particularly for tuberculosis research. TB urgently requires new diagnostic methods (the ones in common use today date from the 19th century), improved treatment drugs and programmes, and a new vaccine (Bacille Calmette-Guérin, the TB vaccine, was developed between 1908 and 1921). Among people living with HIV, TB is the commonest cause of death and over 1.4 million people living with HIV develop TB each year. Activists from among all stakeholders (community, scientists, government, funders, and others) need to join in concerted action to ensure rapid development of diagnostics, drugs, vaccines, and delivery systems to prevent people dying from tuberculosis.

Increasing Civil Society Participation in the National HIV Response: The Role of UNGASS Reporting.


The 2001 Declaration of Commitment on HIV/AIDS provided impetus for strengthening collaboration between government and civil society partners in the HIV response. The biennial UNGASS reporting process is an opportunity for civil society to engage in a review of the implementation of commitments. The article is reporting on the descriptive analyses of the National Composite Policy Index from 135 countries; a debriefing on UNGASS reporting with civil society in 40 countries; and 3 country case studies on the UNGASS process. In the latest UNGASS reporting round, engagement of civil society occurred in the vast majority of countries. The utility of UNGASS reporting seemed to be better understood by both government and civil society, compared with previous reporting rounds. Civil society participation was strongest when civil society groupings took the initiative and organized themselves. An important barrier was their lack of experience with national level processes. Civil society involvement in national HIV planning and strategic processes was perceived to be good, but better access to funding and technical support is needed. Instances remain where there are fundamental differences between government and civil society perceptions of the HIV policy and program environment. How or whether differences were resolved is not always clear, but both government and civil society seemed to appreciate the opportunity for discussion. Collaborative reporting by government and civil society on UNGASS indicators is a small but potentially valuable step in what should be an ongoing and fully institutionalized process of collaborative planning, implementation, monitoring, assessment and correction of HIV responses. The momentum achieved through the UNGASS process should be maintained with follow-up actions to address data gaps, formalize partnerships and enhance active and meaningful engagement.

For full text access click here:
http://journals.lww.com/jaids/Fulltext/2009/12012/Increasing_Civil_Society_Participation_in_the.4.aspx
Editors’ note: Civil society is defined in this article as voluntary associations of citizens that undertake actions in support of people living with or affected by HIV; it does not include the private (profit-making) or public (government) sectors. Civil society involvement in national HIV responses has increased since 2005 but there is room for improvement in virtually all countries if civil society participation is to be truly active and meaningful. One indicator is the number of ‘shadow reports’ from civil society groups dissatisfied with the government reporting on progress. This number has declined from 33 countries in 2006 to 15 countries in 2008, and some of the latter reports were simply providing additional information, as opposed to expressing dissenting views. Although UNGASS reporting is an international accountability tool based on the 2001 Declaration of Commitment, the reporting process itself can be a mechanism to increase civil society engagement in the national HIV response and enhance government accountability to its own citizens.

5. Epidemiology


Mahy M, Warner-Smith M, Stanecki KA, Ghys PD. J Acquir Immune Defic Syndr. 2009; Nov. 52(S1)

In the Declaration of Commitment of the 2001 United Nations General Assembly Special Session on AIDS, all Member States agreed to a series of actions to address HIV. This article examines the availability of data to measure progress toward reducing HIV incidence and AIDS mortality and discusses the extent to which changes can be attributed to programs. Lacking a method to directly measure HIV incidence, trends in HIV prevalence among 15-year to 24-year olds and groups with high-risk behaviours are used as a proxy measure for incidence trends among adults in generalized and concentrated/low-level epidemics, respectively. Although there is limited empirical data on trends in new infections among children, progress in the treatment area is tracked through indicators for the percentage of people who remain on antiretroviral treatment 12 months after initiation and the coverage of antiretroviral treatment. Successive iterations of epidemiological models using surveillance data from pregnant women and groups with high-risk behaviour and data from national household surveys, demographic data and epidemiological assumptions have produced increasingly robust estimates of HIV prevalence, incidence and mortality. Globally, incidence has decreased among adults (accompanied by evidence of changes in behaviour in several countries) and children over the past decade. The decline in AIDS mortality is more recent. On the basis of the underlying logical framework and mathematical models, it is concluded that programs have contributed to a reduction in HIV incidence and AIDS mortality. More data are needed to reliably inform trends in HIV incidence and AIDS mortality in many countries to allow an assessment of progress against national and global targets. In addition, impact evaluation studies are needed to assess the relationship between changes in incidence and mortality and the HIV response and to determine the extent to which these changes can be attributed to specific programmatic interventions.

For full text access click here:

http://journals.lww.com/jaids/Fulltext/2009/12012/Measuring_the_Impact_of_the_Global_Response_t o_the.11.aspx

Editors’ note: The decline in new infections (incidence) reported in the 2009 UNAIDS/WHO Epidemic Update is not translating into lower numbers of people living with HIV (prevalence) because antiretroviral treatment roll-out is reducing mortality. Thus, there are fewer new infections and fewer deaths but the size of the HIV epidemic in absolute numbers continues to grow. This article examines the availability and nature of data to track the HIV epidemic, the modelling undertaken to estimate trends, and the importance of robust evaluations of programmes and policies to explain what has contributed, and what has not, to the changes in incidence that we are observing. Although generally we are on track to be able to know in 2015 whether the HIV epidemic has been ‘halted and reversed’ (Millennium Development Goal 6), this analysis of
6. Men who have sex with men

Anal Sexually Transmitted Infections and Risk of HIV Infection in Homosexual Men.


Jin et al examined a range of common bacterial and viral sexually transmitted infections as risk factors for HIV seroconversion in a community-based cohort of HIV-negative homosexual men in Sydney, Australia. Detailed information about HIV risk behaviours was collected by interview twice yearly. Participants were tested annually for HIV, anal and urethral gonorrhoea and chlamydia, herpes simplex virus types 1 and 2, and syphilis. In addition, they reported annual diagnoses of these conditions and of genital and anal warts. Among 1427 enrolled participants, 53 HIV seroconverters were identified, giving an incidence of 0.78 per 100 person-years. After controlling for number of episodes of insertive and receptive nonseroconcordant unprotected anal intercourse, there were independent associations with anal gonorrhoea (adjusted hazard ratio = 7.12, 95% confidence interval: 2.05 to 24.79) and anal warts (hazard ratio = 3.63, 95% confidence interval: 1.62 to 8.14). Anal gonorrhoea and anal warts were independently associated with HIV acquisition. The added HIV prevention value of more frequent screening of the anus to allow early detection and treatment of anal sexually transmitted infections in homosexual men should be considered.

For abstract access click here: http://www.ncbi.nlm.nih.gov/pubmed/19734801

Editor’s note: For the most part, the anal gonorrhoea diagnosed in this study of men who have sex with men was asymptomatic, suggesting that it was of relatively long standing. It may have caused a low-grade inflammation that would attract HIV target cells. Likewise, anal warts themselves and/or their treatment can disrupt natural defences, allowing HIV easier access to its prey. Given that these two infections were independently associated with HIV acquisition, it is important to assess the potential impact on HIV incidence in men who have sex with men of frequent sexual health screening and treatment of anal gonorrhoea and anal warts.

7. Drug discovery and pharmacokinetics

Novel approaches to inhibiting HIV-1 replication.

Adamson CS, Freed EO. 2009 Antiviral Res. Sep. [Epub ahead of print]

Considerable success has been achieved in the treatment of HIV-1 infection, and more than two-dozen antiretroviral drugs are available targeting several distinct steps in the viral replication cycle. However, resistance to these compounds emerges readily, even in the context of combination therapy. Drug toxicity, adverse drug-drug interactions, and accompanying poor patient adherence can also lead to treatment failure. These considerations make continued development of novel antiretroviral therapeutics necessary. In this article, the authors highlight a number of steps in the HIV-1 replication cycle that represent promising targets for drug discovery. These include lipid raft microdomains, the RNase H activity of the viral enzyme reverse transcriptase, uncoating of the viral core, host cell machinery involved in the integration of the viral DNA into host cell chromatin, virus assembly, maturation, and budding, and the functions of several viral accessory proteins. The authors discuss the relevant molecular and cell biology, and describe progress to date in developing inhibitors against these novel targets.

For abstract access click here: http://www.ncbi.nlm.nih.gov/pubmed/19782103
Editors’ note: Once inside the cell, HIV takes advantage of host cell factors and pathways, harnessing our machinery to promote its own replication. Having described the HIV life cycle, this article briefly reviews the classes of drugs that we currently have (more than 20 antiretroviral drugs have been licensed to date): entry inhibitors (fusion inhibitors and CCR5 antagonists), reverse transcriptase inhibitors (non-nucleoside and nucleoside, i.e. NNRTI and NRTI), protease inhibitors, and integrase inhibitors. Then, accompanied by many colourful figures, the authors present an array of potential new therapeutic targets that include viral-host protein interactions or cellular targets. It will be a challenge for virology and biology (chemical, structural, molecular, and cell) to determine whether we can block HIV’s use of these interactions or cellular targets for multiple steps of its own replication without creating toxicity for us, since we need these proteins and cellular factors for a variety of our own functions.

How much ritonavir is needed to boost protease inhibitors? Systematic review of 17 dose-ranging pharmacokinetic trials.


Ritonavir has been evaluated at boosting doses of 50-800 mg daily with seven protease inhibitors: amprenavir, atazanavir, darunavir, indinavir, lopinavir, saquinavir and tipranavir. Minimizing the boosting dose of ritonavir could improve tolerability and lower costs. A MEDLINE search identified 17 pharmacokinetic trials using different ritonavir doses with protease inhibitors. The dose of ritonavir used was correlated with plasma levels of each boosted protease inhibitor. For the five pharmacokinetic trials of lopinavir/ritonavir, a meta-analysis was used to estimate the effects of lopinavir dose versus ritonavir dose on lopinavir pharmacokinetics. Saquinavir, fosamprenavir and darunavir were boosted equally well by lower (50-100 mg) versus higher doses of ritonavir. Indinavir, tipranavir and lopinavir were boosted more by higher ritonavir doses. Data on atazanavir were inconclusive. The ritonavir dose-dependence of boosting effects did not correlate with their bioavailability or their effects on ritonavir plasma levels. Atazanavir and indinavir raised plasma ritonavir levels by 69-72%, whereas saquinavir had no effects on ritonavir. Darunavir, lopinavir, tipranavir and fosamprenavir all lowered ritonavir plasma levels. For the meta-analysis of lopinavir/ritonavir trials, the 200/150 mg twice daily (b.i.d.) dose of lopinavir/ritonavir (one Meltrex 200/50 mg tablet and one ritonavir 100 mg b.i.d.) showed lopinavir area under the curve and minimum concentration similar to the standard 400/100 mg b.i.d. dose. It may be possible to use three protease inhibitors (saquinavir, amprenavir and darunavir) with lower doses of ritonavir. A 200/150 mg b.i.d. dose of lopinavir/ritonavir could lower costs while maintaining very similar lopinavir plasma levels to the standard dose. New pharmacoenhancer drugs may need to be used at different doses to boost different antiretrovirals.

For abstract access click here:

Editors’ note: A boosted protease inhibitor plus two nucleoside analogues (NRTIs) are recommended by WHO for second line antiretroviral treatment, with atazanavir and lopinavir being the preferred options. For boosted protease inhibitors, an optimal safety profile depends on both the choice of protease inhibitor and the lowest dose of ritonavir possible. The dose-ranging pharmacokinetic trials that are reported in the public domain here suggest that the pharmacokinetics of lopinavir are highly dependent on the dose of ritonavir used, as well as the lopinavir dose. This suggests that a crossover dose-ranging trial of lopinavir/ritonavir would help determine whether 400/100 mg versus 200/150 mg doses, for example, provide the optimum pharmacokinetics with lowest toxicity.
8. Biomedical trial conduct

Microbicides Development Programme: Engaging the community in the standard of care debate in a vaginal microbicide trial in Mwanza, Tanzania.


HIV prevention research in resource-limited countries is associated with a variety of ethical dilemmas. Key amongst these is the question of what constitutes an appropriate standard of health care for participants in HIV prevention trials. This paper describes a community-focused approach to develop a locally-appropriate standard of health care in the context of a phase III vaginal microbicide trial in Mwanza City, northwest Tanzania. A mobile community-based sexual and reproductive health service for women working as informal food vendors or in traditional and modern bars, restaurants, hotels and guesthouses has been established in 10 city wards. Wards were divided into geographical clusters and community representatives elected at cluster and ward level. A city-level Community Advisory Committee with representatives from each ward has been established. Workshops and community meetings at ward and city-level have explored project-related concerns using tools adapted from participatory learning and action techniques e.g. chapati diagrams, pair-wise ranking. Secondary stakeholders representing local public-sector and non-governmental health and social care providers have formed a trial Stakeholders’ Advisory Group, which includes two Community Advisory Committee representatives. Key recommendations from participatory community workshops, Community Advisory Committee and Stakeholders’ Advisory Group meetings conducted in the first year of the trial relate to the quality and range of clinic services provided at study clinics as well as broader standard of care issues. Recommendations have included streamlining clinic services to reduce waiting times, expanding services to include the children and spouses of participants, and providing care for common local conditions such as malaria. Participants, community representatives and stakeholders felt there was an ethical obligation to ensure effective access to antiretroviral drugs and to provide supportive community-based care for women identified as HIV positive during the trial. This obligation includes ensuring sustainable, post-trial access to these services. Post-trial access to an effective vaginal microbicide was also felt to be a moral imperative. Participatory methodologies enabled effective partnerships between researchers, participant representatives and community stakeholders to be developed and facilitated local dialogue and consensus on what constitutes a locally-appropriate standard of care in the context of a vaginal microbicide trial in this setting.

For full text access click here: http://www.biomedcentral.com/1472-6939/10/1

Editors’ note: HIV prevention trials present a number of ethical dilemmas, including that of determining what is the most appropriate standard of care for people found to be ineligible during initial screening for recruitment and for those who develop illnesses during a trial. Is providing the best standard of care coercive and unethical if only research participants can benefit and parallel services cannot be sustained following trial cessation? Should researchers strive to ‘ratchet up’ local standards of care in the communities hosting clinical trials? Effective, participatory community engagement in trial design and ongoing management, as is described here in this microbicide trial, can help stakeholders decide together where researcher obligations to trial participants end and can help ensure that health service delivery is locally-appropriate, acceptable, and effective. Guidance on ethical dilemmas may be found in the UNAIDS/WHO Ethical considerations in biomedical HIV prevention trials. For more on the principles and practice of community engagement consult the UNAIDS/AVAC Good Participatory Practice (GPP) guidelines for biomedical HIV prevention trials. Sharing experiences in resolving ethical dilemmas through meaningful participatory processes helps advance both knowledge and practice.

9. IDU

Retention in Opioid Substitution Treatment: A Major Predictor of Long-Term Virological Success for HIV-Infected Injection Drug Users Receiving Antiretroviral Treatment.


The positive impact of opioid substitution treatment on opioid-dependent individuals with human immunodeficiency virus (HIV) infection is well documented, especially with regard to adherence to antiretroviral therapy. Roux et al used the data from a 5-year longitudinal study of the MANIF 2000 cohort of individuals infected with HIV (as a result of injection drug use) and receiving ART to investigate the predictors of long-term virological success. Data were collected every 6 months from outpatient hospital services delivering HIV care in France. The authors selected all patients who were receiving antiretroviral therapy for at least 6 months (baseline visit) and who had indications for opioid substitution treatment (ie, still dependent on opioids). They selected a total of 113 patients, accounting for a total of 562 visits for all the analyses. Long-term virological success was defined as an undetectable viral load after at least 6 months on antiretroviral therapy. Retention in opioid substitution treatment was defined as the time interval between the last initiation or reinitiation of opioid substitution treatment during antiretroviral therapy follow-up and any given visit on opioid substitution treatment. A mixed logistic model was used to identify predictors of long-term virological success. At baseline, 53 patients were receiving buprenorphine, 28 patients were receiving methadone, and 32 patients were not on opioid substitution treatment. The median duration of opioid substitution treatment was 25 months (range, 3-42 months). In the multivariate analysis, after adjustment for significant predictors of long-term virological success such as adherence to antiretroviral therapy and early virological response, retention in opioid substitution treatment was associated with long-term virological success (odds ratio, 1.20 per 6-month increase; 95% confidence interval, 1.09-1.32). The study presents important evidence of the positive impact of retention in opioid substitution treatment on HIV outcomes. Increasing access to opioid substitution treatment based on a comprehensive model of care for HIV-infected patients who have indications for opioid substitution treatment may foster adherence and ensure long-term response to antiretroviral therapy.

For full text access click here:

Editors’ note: Although people who inject drugs and who adhere to antiretroviral treatment have similar HIV outcomes to people who do not inject drugs, physicians may deny or delay initiation of antiretroviral treatment to active drug users. This is the first study to show that retention in opioid substitution treatment contributes to long-term virological suppression in injecting drug users on antiretroviral treatment. Expanded access to opioid substitutes, in the context of comprehensive care, is known to reduce the use of nonsterile injecting equipment and to increase consistent condom use. Given that opioid substitutes are included in the WHO list of essential medicines, the virological outcomes reported here give added impetus to initiatives to increase access to opioid substitution treatment for people living with HIV who inject drugs.

Expanding the reach of harm reduction in Thailand: Experiences with a drug user-run drop-in centre.


Despite an ongoing epidemic of HIV among Thai people who inject drugs, Thailand has failed to implement essential harm reduction programmes. In response, a drug user-led harm reduction centre opened in 2004 in an effort to expand reduction programming in Thailand. The authors examined experiences with the Mitsampan Harm Reduction Centre (MSHRC) among injecting drug users participating in the Mitsampan Community Research Project (Bangkok).
Multivariate logistic regression was used to identify factors associated with Mitsampan Harm Reduction Centre use. Kerr et al. also examined services used at and barriers to the Mitsampan Harm Reduction Centre. 252 injecting drug users participated in this study, including 66 (26.2%) females. In total, 74 (29.3%) participants had accessed the Mitsampan Harm Reduction Centre. In multivariate analyses, **Mitsampan Harm Reduction Centre use was positively associated with difficulty accessing syringes** (Adjusted Odds Ratio [AOR]=4.05; 95% Confidence Interval [CI]: 1.67-9.80), **midazolam injection** (AOR=3.25; 95%CI: 1.58-6.71), **having greater than primary school education** (AOR=1.88; 95%CI: 1.01-3.52), and was **negatively associated with female gender** (AOR=0.20; 95%CI: 0.08-0.50). Forms of support most commonly accessed included: **syringe distribution** (100%), **food and a place to rest** (83.8%), **HIV education** (75.7%), and **safer injecting education** (66.2%). The primary reason given for not having accessed the Mitsampan Harm Reduction Centre was “didn’t know it existed.” The Mitsampan Harm Reduction Centre is expanding the scope of harm reduction in Thailand by reaching injecting drug users, including those who report difficulty accessing sterile syringes, and by providing various forms of support. In order to maximise its benefits, efforts should be made to increase awareness of the Mitsampan Harm Reduction Centre, in particular among women.

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http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6VJX-4X84JB8-1&_user=3824252&_fmt=&_orig=search&_sort=d&_docanchor=&view=c&_acct=C00005538&_version=1&_userid=3824252&md5=cd60c311efd0c6cede315f8be53ed

**Editors’ note:** Although drug user-led initiatives to provide harm reduction services have been described in North America, Europe, and Australia, the group of drug users who opened this drug-user-run drop-in centre in Bangkok in 2004 with funding from the Global Fund to fight AIDS, Tuberculosis and Malaria were sailing in uncharted waters for Thailand. The Thai Drug Users Network and the Thai AIDS Treatment Action Group (TTAG) collaborated to start the centre which is open six days a week from 10 am to 7 pm and has 500 to 600 visits per month. At the end of the Global Fund grant in 2008, TTAG assumed oversight of the centre, with drug users continuing to run the centre. It is perhaps not surprising that many drug users interviewed were not aware of the centre given obvious difficulties in advertising its services in a context of documented extreme stigma and discrimination. Expanding the scope of this service and increasing the availability of harm reduction services in general in Thailand will require enlightened leadership in order to reduce the risk of HIV acquisition and transmission among Thais who inject drugs.

10. HIV testing


Voluntary counselling and testing for couples is an important HIV-prevention effort in sub-Saharan Africa where a substantial proportion of HIV transmission occurs within stable partnerships. This study aimed to determine the acceptance and effectiveness of couples voluntary counselling and testing as compared to individual voluntary counselling and testing. 1,521 women attending three antenatal clinics in Dar es Salaam were randomized to receive individual voluntary counselling during that visit or couples voluntary counselling with their husbands at a subsequent visit. The proportion of women receiving test results in the couples voluntary counselling and testing arm was significantly lower than in the individual voluntary counselling and testing arm (39 vs. 71%). HIV prevalence overall was 10%. In a subgroup analysis of HIV-positive women, those who received couples voluntary counselling and testing were more likely to use preventive measures against transmission (90 vs. 60%) and to receive nevirapine for themselves (55 vs. 24%) and their infants (55 vs. 22%) as compared to women randomized to individual voluntary counselling and testing. Uptake of couples voluntary counselling and testing is
low in the antenatal clinic setting. Community mobilization and couple-friendly clinics are needed to promote couples voluntary counselling and testing.

For abstract access click here: http://www.ncbi.nlm.nih.gov/pubmed/19763813

Editors’ note: In this study, only 16% of the women randomised to the couples voluntary counselling and testing arm were counselled, tested, and shared results together with their husbands/cohabiting partners. This is an opportunity to learn together about HIV transmission, discuss personal and combined risks, and develop a collaborative plan to prevent further transmission, assisted by a professional. Antenatal clinics are clearly either not perceived by men as male-friendly places or not perceived by couples as couple-friendly places. Given that a considerable proportion of HIV transmission in sub-Saharan Africa is occurring within married or cohabiting couples and given that individual testing and counselling addresses only half of the sexual partnership, strategies to create new social norms to increase the acceptability of couple testing and determine the best venues for it are urgently needed.

11. Basic Science

Orally exposed uninfected individuals have systemic anti-HIV responses associating with partners’ viral load.


The aim of this study was determine whether oral HIV-1 exposure incites a persistent systemic anti-HIV-1 response in exposed uninfected individuals of discordant couples of men who have sex with men, and whether this response associates with HIV-1 exposure measured by viral load in the HIV-positive partners. Plasma samples were collected from exposed uninfected individuals (n = 25), HIV-positive partners (n = 25) and low-risk controls (n = 22). A peripheral blood mononuclear cells-based neutralization assay was used to test these samples against three primary HIV-1 isolates. Self-reported questionnaires described routes of HIV-1-exposure, and clinical records documented viral loads in HIV-positive partners. At enrolment, plasma samples from seven of 25 exposed uninfected individuals neutralized at least two of the three HIV-1 isolates. No samples from the 22 controls neutralized any HIV-1 isolate (P = 0.01). Of these seven exposed uninfected individuals, six retained neutralization capacity during follow-up. Neutralization capacity among exposed uninfected individuals associated with the highest measured viral load of their respective partners (P = 0.01) and also time since highest viral load (P = 0.02). Purified plasma immunoglobulin (Ig) A1-mediated neutralization was observed in six of the seven samples, whereas none of the IgA1-depleted plasma samples neutralized HIV-1. The neutralizing IgA1 was not HIV envelope specific as detected by ELISA and western blot. Orally exposed uninfected men who have sex with men can mount neutralizing anti HIV-1 activity in plasma, mediated primarily by non-HIV envelope-specific IgA1. Neutralization was associated with previous measured highest viral load in the HIV-positive partner, as well as time elapsed since the peak viral load. Neutralization also persisted over time in spite of a continuous low viral exposure.

For abstract access click here: http://www.ncbi.nlm.nih.gov/pubmed/19779318

Editors’ note: In this intriguing study of discordant couples of men who have sex with men, oral mucosal exposure to HIV (measured as the highest observed level of HIV-RNA in each subject’s infected partner) was correlated with the development of a functional anti-HIV response in the plasma. Looking for explanations, the researchers checked for the CCR5 delta 32 deletion that confers protection if both genes are affected but only one individual was homozygous. One of the seven men that had anti-HIV responses subsequently became infected, but with a different clade than the one his partner had. This suggests that the antibodies that were generated, if protective, are not likely to be broadly neutralizing. In any case, the findings of this study have implications for vaccine research because they suggest that low-level mucosal exposure may induce acquired immunity.
12. Influenza and HIV

Pandemic influenza: implications for programs controlling for HIV infection, tuberculosis, and chronic viral hepatitis.


Among vulnerable populations during an influenza pandemic are persons with or at risk for HIV infection, tuberculosis, or chronic viral hepatitis. **HIV-infected persons have higher rates of hospitalization, prolonged illness, and increased mortality from influenza compared with the general population.** Persons with tuberculosis and chronic viral hepatitis may also be at increased risk of morbidity and mortality from influenza because of altered immunity and chronic illness. These populations also face social and structural barriers that will be exacerbated by a pandemic. Existing infrastructure should be expanded and pandemic planning should include preparations to reduce the risks for these populations.

For full text access click here: 
http://ajph.aphapublications.org/cgi/content/full/99/S2/S333?view=long&pmid=19797745

Editors’ note: This article highlights the importance of pandemic influenza plans that include specific actions to reduce the risk of influenza among people living with HIV, tuberculosis or viral hepatitis and maintain continuity of care and prevention services. In the case of HIV, it is critical to prevent disruptions in the supply of antiretroviral drugs and to anticipate and mitigate personnel shortages to avoid the erratic dosing and sub therapeutic drug levels that can lead to disease progression and viral resistance. Improving rates of annual vaccination against seasonal influenza among people living with HIV, their caretakers, and health care providers is an obvious step. The higher risk of complications among young people with chronic medical conditions, in the case of the H1N1 influenza, underscores the importance of receiving the H1N1 vaccine if this description fits you.

13. Economics


This paper estimates the economic impact of HIV on the KwaZulu-Natal province and the rest of South Africa. Thurlow et al extended previous studies by employing: an integrated analytical framework that combined firm surveys of workers’ HIV prevalence by sector and occupation; a demographic model that produced both population and workforce projections; and a regionalized economy-wide model linked to a survey-based micro-simulation module. This framework permits a full macro-microeconomic assessment. Results indicate that **HIV greatly reduces annual economic growth, mainly by lowering the long-run rate of technical change.** However, impacts on income poverty are small, and inequality is reduced by HIV. This is because high unemployment among low-income households minimises the economic costs of increased mortality. By contrast, slower economic growth hurts higher income households despite lower HIV prevalence. They conclude that the increase in economic growth that results from addressing HIV is sufficient to offset the population pressure placed on income poverty. **Moreover, incentives to mitigate HIV lie not only with poorer infected households, but also with uninfected higher income households.** Their findings reveal the substantial burden that HIV places on future economic development in KwaZulu-Natal and South Africa, and confirms the need for policies to curb the economic costs of the pandemic.

For full text access click here: 
http://www.jiasociety.org/content/12/1/18

Editors’ note: This macro-microeconomic assessment of the present and future impact of HIV on the KwaZulu-Natal economy used survey data on HIV prevalence among managers, skilled
workers, and labourers in 15 companies across four sectors: agriculture, manufacturing, tourism, and transport sectors. These findings were used to calibrate a demographic model and then its projections were imposed on a dynamic computable general equilibrium model linked to a household-survey based micro-simulation model. Sound complicated? Yes, it definitely is, however this approach integrating demographic, economy-wide, and survey-based models produces striking estimates. The Gross Domestic Product (GDP) growth rate in KwaZulu-Natal is lowered by 1.6% per year and although that does not sound like much, it results in an economy that would be 43% smaller in 2025 than it would be in the absence of HIV. These are the kinds of results that policy makers understand and that can motivate them to mobilise investments to curb HIV transmission and improve treatment access.

That was *HIV this week*, signing off.

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**Editors’ notes on journal access**

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